



Cardioprotective Effect of Hydroethanolic Extract *Artocarpus altilis* In Isoproterenol Induced Myocardial Rats

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Abstract

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Myocardial infarction is a disease that occurs when the blood supply to a part of the heart is interrupted, causing death of heart tissue. In this study the cardioprotective effect of the hydroethanolic extract of *Artocarpus altilis*(at the dosage of 250 mg/kg body weight for 30 days) against Isoproterenol induced Myocardial rats were studied and also compared with the standard drug Propranolol. Myocardial Infarction was induced with a single dose of ISO (85 mg/kg) on the 29th and 30th day. At the end of 30 days (i.e., on the day 31st), serum and heart tissues were collected and cardiac marker enzymes such as creatine kinase - MB (CK-MB), Aspartate transaminase (AST), Alanine Transaminase (ALT) and Lactate dehydrogenase (LDH) in serum were evaluated. Histopathological observations of heart tissues were performed. Administration of ISO in control rats showed a significant increase in serum CK-MB, AST, ALT, LDH. Rats treated with hydroethanolic extract of *Artocarpus altilis* (250 mg/kg body weight) restored the levels of CK-MB, AST, ALT and LDH nearer to the level of normal rats. The histopathological studies also showed that Plant extract significantly minimized the damage induced by isoproterenol. Thus the current study indicated the Cardioprotective activity of *Artocarpus altilis* in Isoproterenol induced myocardial rats.

Keywords: Myocardial Infarction, *Artocarpus altilis*.

INTRODUCTION

Myocardial Infarction (MI) is an acute condition of the necrosis of the myocardium that occurs as a result of imbalance between coronary blood supply and myocardial demand [1]. Congestive heart failure (CHF) after MI is a common clinical syndrome with a grave prognosis. Loss of contracting myocardium due to MI results in a chronic increase in the workload of the remaining viable myocardium. In this regard, data from animal experiments have suggested that increases in free radical formation and subsequent oxidative stress associated with the occurrence of a relative deficit in the endogenous antioxidant reserve may be one of the mechanisms for the development of CHF [2]. Ischemia is regarded as the main mechanism that induces myocardial injury and subsequent cardiomyocyte (CM) loss. The low regenerative capacity of CM's results in scar formation and a decrease in pump force [3]. Complications of MI include Arrhythmia, Congestive heart failure, Cardiogenic shock, Ventricular aneurysm, Pericarditis, Dressler syndrome and pulmonary embolism. Increased oxidative stress and the generation of the free oxygen radicals can result in modification of LDL to oxidized LDL that could lead to Atherosclerotic lesions [4]. L-Isoproterenol (ISO), a synthetic catecholamine causes myocardial cell damage when administered in large doses. Repeated subcutaneous administration of ISO also produces myocardial necrosis in rats and serves as a good model for acute MI [5]. Propranolol is a medication of the beta blocker type. It is used to treat high blood pressure, a number of types of irregular heart rate, thyrotoxicosis, capillary hemangiomas, performance anxiety, and essential tremors [6].



Figure 1: Fruit of *Artocarpus altilis*

Artocarpus altilis belongs to the family Moraceae and it is commonly called as Bread fruit. *Artocarpus* species consists of phenolic compounds. *Artocarpus* extracts and metabolites from leaves, stem, fruit and bark contain numerous beneficial biologically active compounds and these compounds are used in the various biological activities including antibacterial, antitubercular, anti-viral, anti-fungal, anti-platelet, anti-arthritic, tyrosinase inhibitory and cytotoxicity [7]. Hence, in the current study, the possible role of *Artocarpus altilis* (250 mg/kg, per oral [po]) and Propranolol (10 mg/kg, po) in cardioprotection against ISO-induced cardiotoxicity was examined.

MATERIALS AND METHODS

Chemicals

Isoproterenol was purchased from Sigma-aldrich and all the chemicals and drug were of analytical grade.

Plant Collection

The fruits of *Artocarpus altilis* were collected from Namakkal district, Tamilnadu. The plants were identified and authenticated (No: BSIS/RC/5/23/2016/Tech) by the taxonomist, at Botanical Survey of India (BSI), Agricultural University, Coimbatore, Tamilnadu.

Preparation of *artocarpus altilis* extract

The fruits of the plant *Artocarpus altilis* were collected, dried and ground to coarse powder. The coarse powder was extracted using 50 % ethanol (1:3) and kept in a dark room for 72 hours with intermittent shaking. Then the extracts were evaporated to dryness using rotator evaporator. Crystals obtained were stored in desiccator and orally administered to the experimental rats for the treatment of myocardial infarction [4].

Animals

Male *Albino Wistar* rats weighing about 120-150g procured from Kovai Medical Centre Research (KMCH), Coimbatore, Tamilnadu were used for the study. The animals were housed in polypropylene cages and maintained in controlled temperature with 12 hours period of light and dark and fed with standard rat feed and water under hygienic condition [5]. The experiment was carried out as per the guidelines of the committee for the purpose of control and supervision of experiments on animals, India and approved by the Institutional Animal Ethics Committee (IAEC) (353/2017/IAEC).

Experimental setup

The experimental rats were divided into 4 groups of 6 animals (Table 1) in each group [5]

Table 1: Experimental setup

Groups	Experimental animals	No of rats
Group I	Normal rats	6
Group II	Isoproterenol induced (85 mg/kg)	6
Group III	Propranolol (10 mg/kg b.w) + Isoproterenol	6
Group IV	Crude extract of plant(250mg/kg) + Isoproterenol	6

After pretreatment with *Artocarpus altilis* (250 mg/kg b.w orally) and propranolol (10 mg/kg b.w) for 4 weeks, the experimental animals were administered with subcutaneous injection of ISO (85 mg/kg per day, for 2 days at an interval of 24 hours *i.e.*, 29 or 30th day) to induce MI. At the end of the experimental period that is, 18 hours after the second dose of ISO injection, all the rats were anesthetized and sacrificed under mild anesthesia. Blood was collected through heart puncture and the serum separated was used for the determination of cardiac marker enzymes. The heart tissue was excised immediately and washed with ice-cold isotonic saline. The heart tissue and the serum were used for the further biochemical analysis. The isolated hearts are used for Histopathological examinations [5].

BIOCHEMICAL ANALYSIS

The collected serum were used for the estimation for Creatine Kinase - MB (CK-MB), Aspartate Transaminase (AST), Alanine Transaminase (ALT) and Lactate Dehydrogenase (LDH) using commercially available (AUTOSPAN diagnostic) kits according to manufacturer protocol.

HISTOPATHOLOGICAL ANALYSIS

The heart excised out was washed in saline (0.9% NaCl) and tissues were immediately fixed in 10% buffered formalin solution. After fixation, tissues were embedded in paraffin and serial sections were cut and each section was stained using hematoxylin and eosin. After repeated dehydration and cleaning, the sections were mounted and observed under light microscope with magnification of 100x for histological changes [8].

STATISTICAL ANALYSIS

Data were expressed as mean \pm SD (Standard Deviation). Statistical analysis was performed by using Student "t" test using R- Statistical Computing and Graphical Tools (formerly AT & T, Lucent technology). The probability of $p < 0.05$ was considered to be significant.

RESULTS AND DISCUSSION

Effect of *Artocarpus altilis* on Cardiac Marker Enzymes

Isoproterenol - induced myocardial rats showed a significant increase in the levels of CK-MB, LDH, AST and ALT in serum, confirms the onset of myocardial necrosis produced by isoproterenol. The high dose of isoproterenol has ability to destroy myocardial cells and increases the levels of cytosolic enzymes such as CK-MB, LDH, AST and ALT. So amount of enzymes released serve as a diagnostic marker for myocardial tissue damage [9].

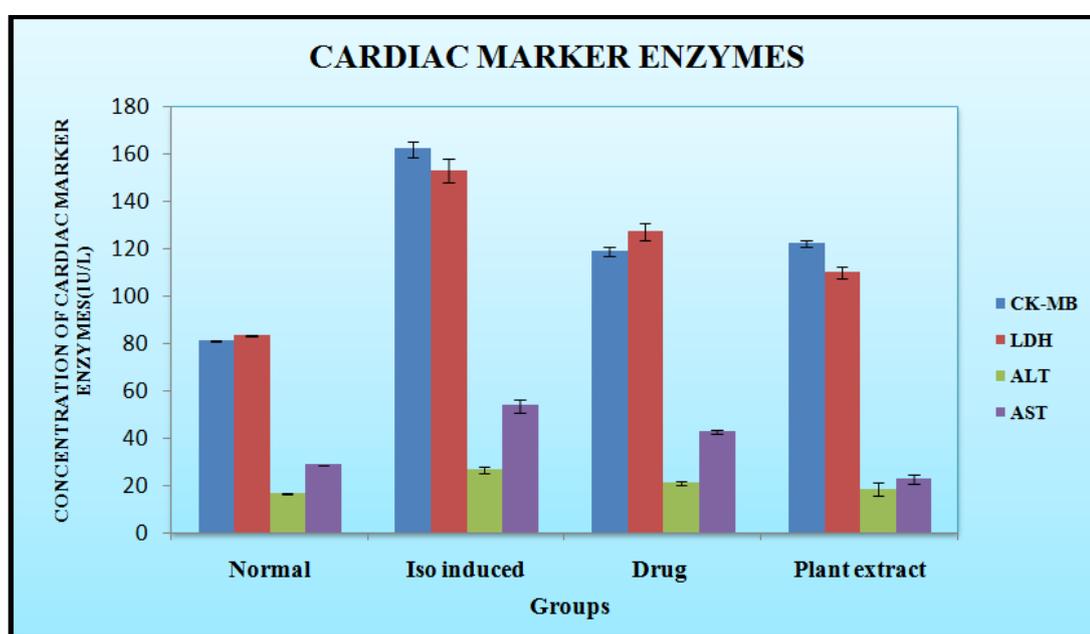


Figure 1: Effect of *Artocarpus altilis* Levels of CK-MB, LDH, AST, ALT in serum of control and experimental rats

Artocarpus altilis pretreatment significantly decreased the levels of CK-MB, LDH, AST and ALT in the serum of ISO induced myocardial rats as shown in figure 1, which may be due to the phenolic compounds present in it. Previous studies have also reported the decrease of these cardiac enzymes after the pretreatment with the plant extract ^[10].

Histopathological studies

Histological observations (Figure 2) showed no pathological changes in myocardium in control rats, whereas in the isoproterenol induced rats showed severe tissue degeneration and necrosis. Pretreatment with *Artocarpus atillis* (Group IV) reversed the changes showing normal tissues with mild degeneration.

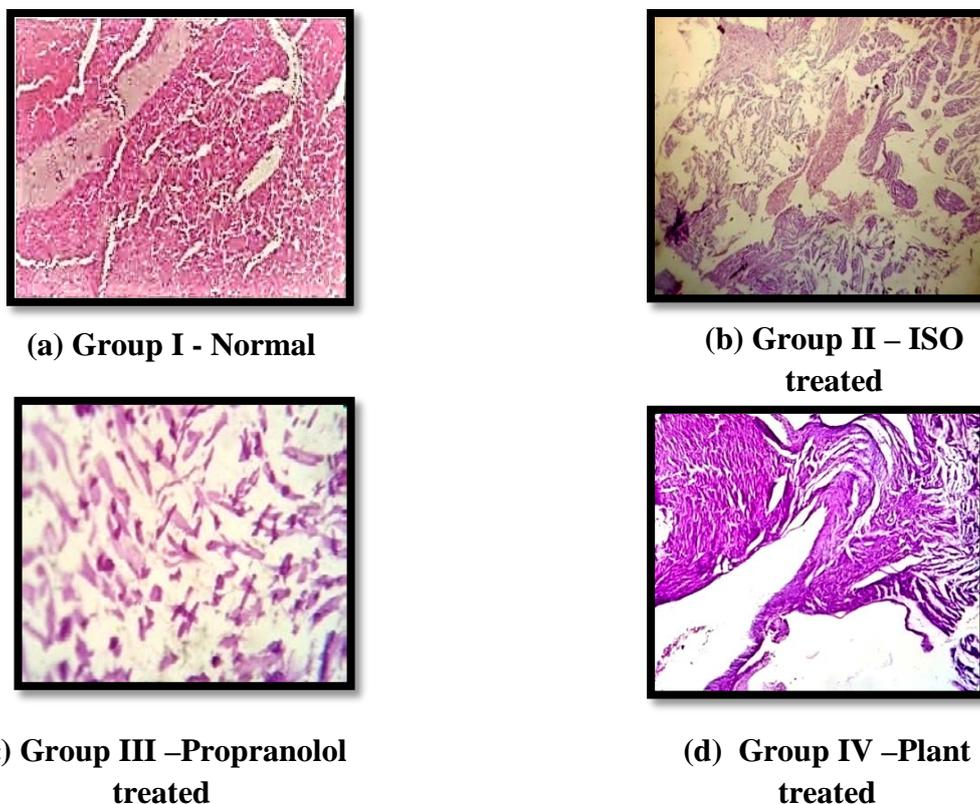


FIGURE 2: HISTOPATHOLOGICAL OBSERVATION OF HEART

Figure 2: Histopathological observation of heart:- (a) **Group I:** Normal architecture of heart, (b) **Group II** (ISO induced): Severe tissue degeneration and necrosis, (c) **Group III** (Propranolol): Mild tissue degeneration and necrosis, (d) **Group IV** (*Artocarpus altilis* extract): Moderate tissue regeneration and necrosis.

CONCLUSION

In summary, the present study implies that the hydroethanolic extract of *Artocarpus altilis* showed a significant decrease in the elevated cardiac marker enzymes which may be due to the phytochemical compounds present in it. The histological findings suggested that, the heart tissues affected by isoproterenol were recovered by the administration of *Artocarpus altilis*. So it has been concluded from the biochemical and histopathological studies that the *Artocarpus altilis* at 250 mg/kg of body weight produced a significant cardioprotection in isoproterenol induced myocardial rats. Thus, our study clearly indicated a significant cardioprotective activity of hydroethanolic extract of *Artocarpus altilis*. Further research is required to isolate the respective bioactive compound responsible for the cardioprotective effect.

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